Smoking Cessation in the Oncology Setting

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www.easternhealth.ca
Disclosures

- There are no financial or educational disclosures
Objectives

• Present evidence as to the clinical and economic benefit of smoking cessation after a cancer diagnosis

• Demonstrate the impact of continued smoking upon cancer treatment

• Highlight work being planned to integrate smoking cessation in an ambulatory oncology setting

• Demonstrate the supportive role of primary care providers in smoking cessation after a cancer diagnosis
Overview

• Cancer Care Program
• The Tobacco Addiction
• Impact on Cancer Treatment
• Benefits of Smoking Cessation After a Cancer Diagnosis
• Pharmacotherapy
• Tobacco Cessation and Relapse Prevention in Cancer Care
Cancer Care Program

• The Cancer Care Program operates out of the Dr. H. Bliss Murphy Cancer Centre in St. John’s
  – Regional Cancer Centres in Gander, Grand Falls-Windsor and Corner Brook

• Chemotherapy provided in ~ 20 sites across NL

• 51 sites with tele-oncology

• Approximately 200 health care providers
  – Oncologists, physicians, nursing, social work, medical physics, radiation therapy, nutrition, clerical support, administration, cancer registry, IT
2016 Canadian Cancer Statistics (NL)

New cases:
- Males: 2,000
- Females: 1,900
- Total: 3,900 (ASI: 610.7/100,000)*

Deaths:
- Males: 780
- Females: 670
- Total: 1,450 (ASM: 228.7/100,000)*
Lifetime possibility of getting cancer

Tobacco & Cigarette Smoke

- Over 7000 constituents in cigarette smoke
- 60+ known carcinogens
- ++ additives
  - Enhance consumption
  - Increase flavor
  - Increase addiction
Cigarette smoking produces a rapid distribution of nicotine to the brain, with drug levels peaking within 10 seconds of inhalation. The acute effects of nicotine dissipate within a few minutes, causing the need to continue repeated intake throughout the day.
The Addiction: Molecular and Behavioral

- Smoking cues, stress
- Neural plasticity
  - Conditioned learning
- Release of dopamine and other neurotransmitters
  - Pleasure, stimulation, mood modulation
- Craving
- Cigarette smoking
- Nicotine spike
- Activated nAChRs
  - Acute tolerance
- Desensitized nAChRs
  - ↑ Nicotine
- Inactive nAChRs
  - ↓ Nicotine
- Reduced levels of dopamine and other neurotransmitters
- Withdrawal symptoms
  - Hedonic dysregulation
Tobacco: A Powerful Addiction

**Probability of dependence after trying a substance at least once**

<table>
<thead>
<tr>
<th>Substance</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>32%</td>
</tr>
<tr>
<td>Heroin</td>
<td>23%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>17%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>15%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>11%</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>9%</td>
</tr>
<tr>
<td>Cannabis</td>
<td>9%</td>
</tr>
<tr>
<td>Analgesics</td>
<td>8%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>4%</td>
</tr>
</tbody>
</table>

*Stahl’s Essential Psychopharmacology, 3rd ed. 2008*
Tobacco & Cancer

• Largest single contributor to cancer risk
• Smoking contributes to 30% of all cancer deaths
• Smoking accounts for approximately 85% of lung cancer deaths
• Sufficient scientific evidence to link tobacco causally to 15 other cancers:
  – oral cavity, nasal cavity and paranasal sinuses, pharynx, larynx, esophagus, stomach, liver, pancreas, cervix, ovary, kidney, ureter, bladder, bowel, acute myeloid leukemia
• Some limited evidence for a link between tobacco smoking and breast cancer

• Studies between 1990-2012
  – About 400 studies with over 500,000 patients

• Evaluation of smoking effects on:
  1. Overall mortality/survival
  2. Cancer-specific mortality/survival
  3. Response to treatment
  4. Toxicity of treatment
  5. Cancer recurrence
  6. Risk of second primaries
Conclusions

– In cancer patients and survivors, the evidence is sufficient to infer a *causal relationship* between cigarette smoking and *adverse health outcomes*. Quitting smoking improves the prognosis of cancer patients.

– In cancer patients and survivors, the evidence is sufficient to infer a *causal relationship* between cigarette smoking and *increased all-cause mortality and cancer-specific mortality*. 
• In cancer patients and survivors, the evidence is sufficient to infer a causal relationship between cigarette smoking and increased risk for second primary cancers known to be caused by cigarette smoking, such as lung cancer.

• In cancer patients and survivors, the evidence is suggestive but not sufficient to infer a causal relationship between cigarette smoking and the risk of recurrence, poorer response to treatment, and increased treatment-related toxicity.
Negative Associations of Smoking
(one or more negative association)

- **Hematologic (n=17)**
  - Significant: 88%
  - Non-significant: 12%

- **Breast (n=31)**
  - Significant: 74%
  - Non-significant: 26%

- **Gynecologic (n=21)**
  - Significant: 81%
  - Non-significant: 19%

- **Genitourinary non-prostate (n=23)**
  - Significant: 83%
  - Non-significant: 17%

- **Prostate (n=17)**
  - Significant: 94%
  - Non-significant: 6%

- **Gastrointestinal (n=37)**
  - Significant: 78%
  - Non-significant: 22%

- **Lung (n=157)**
  - Significant: 88%
  - Non-significant: 12%

- **Head/Neck (n=60)**
  - Significant: 88%
  - Non-significant: 12%

- **Multiple (n=10)**
  - Significant: 100%
  - Non-significant: 0%

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## The 2014 SGR: Outcome Estimates

<table>
<thead>
<tr>
<th>Effect</th>
<th>Studies</th>
<th>Associations (Significant)</th>
<th>RR Magnitude (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Mortality</td>
<td>159</td>
<td>87% (62%)</td>
<td>Current: 1.51</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Former: 1.22</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>62</td>
<td>77% (42%)</td>
<td></td>
</tr>
<tr>
<td>Cancer Related Mortality</td>
<td>58</td>
<td>79% (59%)</td>
<td>Current: 1.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Former: 1.03</td>
</tr>
<tr>
<td>Second Primary</td>
<td>26</td>
<td>100% (100%)</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>51</td>
<td>82% (53%)</td>
<td>Current: 1.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Former: 1.15</td>
</tr>
<tr>
<td>Response</td>
<td>16</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>82</td>
<td>94% (80%)</td>
<td></td>
</tr>
</tbody>
</table>

Sometimes, even if I stand in the middle of the room, no one acknowledges me.
Tobacco Cessation and Cancer Care

• Cigarette smoke initiates tumor growth and may promote tumor progression.
• Stopping tobacco use is one of the best things a patient can do to help their cancer treatment.
• The US Surgeon General indicated that becoming tobacco free can improve outcomes by ~ 40%.
Tobacco Cessation and Cancer Care

• Evidence supports Smoking cessation becoming a standard of care within any cancer treatment plan

• It is argued that If you are able to treat with chemotherapy and/or radiotherapy for the purpose of extending survivorship then we need to consider a patients smoking history and offer smoking cessation
“... the evidence is clear that tobacco use in patients with cancer leads to...”

- decreased treatment efficacy and safety
- decreased survival
- decreased quality of life
- increased treatment-related toxicity
- increased risk of cancer recurrence
- Increased risk of second primary tumours
Clinical Evidence

• “Data suggest that tobacco cessation can improve outcomes and survival in patients with cancer, yet full execution of evidence-based cessation interventions is infrequent in oncology settings.”
  – Dr. Graham Warren, The Paradigm Shift
Impact on Cancer Treatment

• There are several treatment options
  • Surgery
  • Systemic Therapy
  • Radiation Therapy
  • Palliative Care

• Continued smoking after a cancer diagnosis and during active treatment has a significant impact on outcomes and treatment side effects
# Tobacco use & treatment side effects

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Radiation</th>
<th>Surgery</th>
</tr>
</thead>
</table>
| • Exacerbation of side effects including:  
  • Immune suppression  
  • Weight loss  
  • Fatigue  
  • Pulmonary and cardiac toxicity  
  • Increased incidence of infection  
  • May alter the metabolism and/or mechanism of action of chemotherapy making it less effective | • Reduced treatment efficacy  
  • Increased toxicity and side effects to include:  
  • Dry Mouth (Xerostomia)  
  • Oral mucositis (mouth sores)  
  • Loss of taste  
  • Pneumonitis  
  • Soft tissue and bone necrosis  
  • Poor voice quality | • Increased complications from anesthesia  
  • Pulmonary complications  
  • Poor wound healing  
  • Increased risk of infection |

Eastern Health
Smoking and Chemotherapy

- **Erlotinib (e.g. NSCLC and Pancreas)**
  - Lower overall response in smokers vs never smokers
  - Require twice the normal dose to produce needed circulating levels in smokers versus non-smokers
    • Sheppard et al. (July 14, 2005). NEJM 353: 123-132.

- **Irinotecan (e.g. Colorectal cancer and SCLC)**
  - Smokers had ~40% lower systemic exposure to the active metabolite SN-38 compared to non-smokers
Smoking and Molecular Therapy

• Study by Vincenzi (2009) demonstrated that active smoking is associated with less clinical benefit (response plus stable disease in 54% versus 88%) than non-smokers.

• Cetuximab (eg: colorectal and head and neck) cigarette smoking may be responsible for a decrease in the response rate and lead to a lower time to progression (of tumor) from cetuximab-based treatments for advanced colorectal cancers patients among smokers.
  – Vincenzi et al. (August 2009). Biological Therapy, 945-949.
Smoking & Radiation Therapy

- Smokers who continue to smoke during XRT have a significantly lower rate of complete response to radiation therapy (45% vs 74%) and 2-year survival (39% vs 66%)
- Recent quitters were more like long-term quitters than those who continued to smoke in terms of their likelihood of surviving at 18 months
- Browman GP at al. NEJM 1993
  - Dr. Jinka Sathya, Radiation oncologist at the DBMCC co-author
Smoking and Therapeutic Response

CS= continued smoking  RT= radiation therapy

Warren, GM Key note presentation, January 2017
Tobacco Cessation

• Most effective
  – behavioral therapies, non-prescription and prescription medications are used in combination.

• A multidisciplinary approach is crucial

• Tobacco cessation models are brief and goal directed
  – 5A’s
  – 3A’s
  – 2A’s 1R

• Tobacco Cessation = Change Management
Impact on Cancer Centers

• Smoking cessation is a cost effective method to decrease recurrence risk and improve treatment outcomes
• Patients have the opportunity maximize the benefit of their cancer treatment with support from smoking cessation clinics
• Avoiding 2nd line cancer therapy improves quality of life and is cost effective
Impact on Cancer Centers

Smoking and 1st Line Treatment Failure
(20% current smoking rate, 30% baseline failure rate in nonsmokers)

Warren, GM Keynote Presentation, January 2017
# Impact on Cancer Centers

Excess 1<sup>st</sup> Line Treatment Failure and Costs due to Smoking

<table>
<thead>
<tr>
<th>Annual Patient Volume (APV)</th>
<th>RR 1.2</th>
<th>RR 1.4</th>
<th>RR 1.6</th>
<th>RR 1.8</th>
<th>RR 2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>36</td>
<td>42</td>
<td>48</td>
<td>54</td>
<td>60</td>
</tr>
<tr>
<td>1000</td>
<td>72</td>
<td>84</td>
<td>96</td>
<td>108</td>
<td>120</td>
</tr>
<tr>
<td>2000</td>
<td>144</td>
<td>168</td>
<td>192</td>
<td>216</td>
<td>240</td>
</tr>
<tr>
<td>4000</td>
<td>288</td>
<td>336</td>
<td>384</td>
<td>432</td>
<td>480</td>
</tr>
<tr>
<td>8000</td>
<td>576</td>
<td>672</td>
<td>768</td>
<td>864</td>
<td>960</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Line Treatment Cost (per patient)</th>
<th>RR 1.2 500 APV</th>
<th>RR 1.6 2000 APV</th>
<th>RR 2.0 8000 APV</th>
</tr>
</thead>
<tbody>
<tr>
<td>$10K</td>
<td>$360K</td>
<td>$1,920K</td>
<td>$9,600K</td>
</tr>
<tr>
<td>$25K</td>
<td>$900K</td>
<td>$4,800K</td>
<td>$24,000K</td>
</tr>
<tr>
<td>$50K</td>
<td>$1,800K</td>
<td>$9,600K</td>
<td>$48,000K</td>
</tr>
<tr>
<td>$100K</td>
<td>$3,600K</td>
<td>$19,200K</td>
<td>$96,000K</td>
</tr>
<tr>
<td>$400K</td>
<td>$14,400K</td>
<td>$76,800K</td>
<td>$384,000K</td>
</tr>
</tbody>
</table>
Smoking Cessation and Relapse Prevention

• Offer a best practice smoking cessation and relapse prevention program in an ambulatory oncology setting
• Support available to cancer patients receiving active treatment
• Pilot program
  – Head/neck and lung cancer patients
  – Patients offered clinical appointment, medication, and behavioral support
  – Family members offered behavioral support
Key Deliverables to Planning a Cessation Program

- Program Model and Algorithm
- Best Practice review of other programs
- Relationship Building (Primary Care Providers)
- Resource development:
  - Clinical guidelines
  - Patient brochure, guidebook
  - Educational presentations
  - Communications strategy
  - Pharmacotherapy business case
  - Educational opportunities
  - Program cost estimates
  - Program Sustainability Model
Best Practice
Smoking Cessation

Screen
- Ask
- Advise
- Referral

Counsel
- Clinical appointment
- Pharmacotherapy
- Behavioral Therapy

Follow-up
- Clinical follow up Appointment
- Adjust Pharmacotherapy
- PCP Support
Pharmacotherapy Considerations in Oncology

NRT
- May irritate oral mucosa
- With head and neck cancers may exacerbate condition
- Contraindicated for pre-operative surgery

Varenicline (Champix)
- Dosage considerations for patients experiencing nausea
- No evidence on safety/efficacy
- Best to use with behavioral counselling

Bupropion (Zyban)
- May reduce appetite
- Concurrent use of tamoxifen or procarbazine is contraindicated
- Anxiety may increase

Combination NRT and medications
- The addition of nicotine patch to Varenicline did not cause significant changes in side effect profiles
- Side effects of combination therapy of the patch and Bupropion were not significantly different versus bupropion alone
Pharmacotherapy Options

Patient screened

1st 4 weeks

Combo NRT
Nicotine Patch + Short acting NRT (gum, inhaler, lozenge)

Varenicline
(Champix)

Weeks 5-12
If previous not working

Varenicline + NRT

Bupropion (Zyban) + NRT

Bupropion

Adopted from Pharmacotherapy Options from the Centre for Addictions and Mental Health (CAMH)
Motivation Interviewing: Change Management

- **Pre Contemplation**: Not thinking about change
- **Contemplation**: Thinking about change but undecided re need to change
- **Preparation**: Where the individual shows intent to change & starts to plan for change
- **Maintenance**: Maintaining the changes made
- **Action**: The individual is motivated & works with others to start to effect change
- **Lapse/Relapse**: This is an important aspect of change & can lead to a return to behaviours of concern
- **Lasting Change**: Sustaining the changes made over time
## Precautions – First Line Therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral NRT (gum, lozenge, inhaler)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy and radiation therapy</td>
<td>Use with caution if mouth sores</td>
</tr>
<tr>
<td>Head and neck cancer diagnosis</td>
<td>May exacerbate condition</td>
</tr>
<tr>
<td>Pending surgery, treatment, reconstruction</td>
<td>Stop using at least 2 weeks in advance (recommended for NRT patch as well)</td>
</tr>
<tr>
<td>Tooth extraction / dentures</td>
<td>Use of gum is difficult</td>
</tr>
</tbody>
</table>

Source: Aubin et al., 2014.
## Precautions – First Line Therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy to latex</td>
<td>Latex-free nicotine patches are available</td>
</tr>
<tr>
<td>Sleep disorders and insomnia</td>
<td>May worsen, but is better than smoking</td>
</tr>
<tr>
<td>Untreated coronary artery disease, unstable angina / palpitations</td>
<td>May worsen, but is better than smoking</td>
</tr>
</tbody>
</table>

Source: Aubin et al., 2014.
# Precautions – First Line Therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varenicline</td>
<td>Safe, favorable risk/benefit ratio for use</td>
</tr>
</tbody>
</table>

Neuropsychiatric and cardiovascular effects

Source: Aubin et al., 2014.
Precautions – Second Line Therapy

Varenicline + NRT
• The addition of nicotine patch to varenicline did not cause significant changes in side effect profiles of patients

Bupropion + NRT
• Several unwanted side effects more common with bupropion than NRT (e.g. disturbed sleep, dry mouth, headaches, nausea)
• Side effects of combination therapy were not significantly different versus bupropion alone

Sources: NCCN, 2015; Aubin et al., 2014; Karam-Hage et al., 2014
Role of Primary Care Provider

• Prior to consultation at the cancer program asking and advising patients to quit smoking gives them a head start for their cancer treatment plan.
• Primary Care Providers play a critical role in a cancer patients transition into survivorship.
• Communication between the cancer program and the Primary Care Provider is important to ensure post treatment preventative care.
Role of Primary Care Provider

• Although acutely aware of the dangers of smoking and tobacco use, Primary care providers must become champions of post treatment cessation
• Encourage patients to continue to be smoke free
• Primary Care Providers will be notified that patients have received cessation support at the cancer program.
• Continue to ask about smoking status
• Assist in accessing additional cessation supports post cancer treatment
References


• Vincenzi B1, S. D. (August 2009). Cigarettes smoking habit may reduce benefit from cetuximab-based treatment in advanced colorectal cancer patients. Biological Therapy, 945-949.

Questions
Thank you!

I quit.

It’s never too late.